

White (J.W.) & Wood (H.C.)

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CONTRIBUTIONS TO THE DISCUSSION  
ON THE  
DIAGNOSTIC VALUE  
OF THE  
TOLERANCE OF THE IODIDES IN SYPHILIS,  
BETWEEN

J. WILLIAM WHITE, M.D., AND H. C. WOOD, M.D.

BY

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CONTRIBUTIONS TO THE DISCUSSION  
ON THE  
DIAGNOSTIC VALUE  
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TOLERANCE OF THE IODIDES IN SYPHILIS.

DR. H. C. WOOD, Editor of the THERAPEUTIC GAZETTE :

DEAR DOCTOR,—In the December number of the THERAPEUTIC GAZETTE were published my paper on "The Diagnostic Value of the Tolerance of the Iodides in Syphilis," your reply, under the title of "The Iodide of Potassium in Syphilis," and my further comments, "Iodism and Syphilis," which closed the discussion.

As the same number of the GAZETTE contained an editorial request for opinions upon the subject, it occurred to me that an expression of the views of a number of well-known physicians, with special experience in regard to the matter, would be of interest to all those who were already familiar with the opposing theories.

I accordingly wrote to fifteen gentlemen, as follows :

" 1810 SOUTH RITTENHOUSE SQUARE,  
" PHILADELPHIA, December 28, 1888.

" MY DEAR DOCTOR,—Will you do me the favor, after reading the pamphlet which I send you by this mail, of telling me your opinion as to the question at issue? And, if you can spare the time, will you kindly give me your reasons for that opinion? I intend to publish the replies received from a dozen of the best-known syphilitologists and neurologists of the country.

" I need scarcely say that I want to hear from you whether you agree with my views or not. You will greatly oblige me if you can send me an answer at an early date.

" Please believe me, with sincere respect,  
" Yours very truly."

In reply I have thus far received the twelve

communications which I herewith enclose, and which I send you for publication.

Very sincerely,

J. WILLIAM WHITE.

February 12, 1889.

" MONTREAL, January 10, 1889.

" MY DEAR DOCTOR,—I have been much interested in the important questions discussed so ably by Dr. Wood and yourself in the THERAPEUTIC GAZETTE for December.

" From a careful perusal of Dr. Wood's paper I come to the conclusion that he maintains the following propositions as practically proven :

" I. That in nearly all cases of chronic syphilis, especially in syphilis of the nervous system, the administration of the iodide of potassium is not attended by iodism in any of its forms.

" II. That the administration of the iodide of potassium in health and in diseases other than those of a syphilitic character is almost universally attended by iodism.

" I have always looked upon iodism occurring in the course of the iodide-treatment of syphilis as exceptional, the rule being that it is far from common to find iodism, but the exceptions to this rule are, in my opinion, numerous enough to take away all value from the proposed 'therapeutic test.'

" It appears to me that iodism is simply a proof that the elimination of the drug is to some extent effected by the skin and mucous membranes, and that the tolerance of large



doses for long periods is explained by the eliminating surfaces becoming accustomed to the irritating effects of the drug. If any part of the cutaneo-mucous tract is the *locus minoris resistentiae*, we have symptoms of irritation of that part.

"As a rule, to which, however, there are no doubt many exceptions, the more active the draining powers of the kidneys, the less likely is there to be iodism, because there is less elimination through the skin and mucous membranes. The less the elimination through the kidneys, the greater the danger of iodism. There is abundant clinical proof for the last statement.

"Dr. George Johnson\* has especially called attention to the frequency of iodism in cases of chronic Bright's disease.

"There can be no lack of evidence to prove the truth or falsity of the assertion,† that 'the vast majority . . . of persons who are free from syphilitic infection cannot take doses of over 10 grains of the iodide three times a day without the production of iodism, unless as the result of the habitual use of the remedy. When iodides are tolerated by the normal individual, such individual is said to have an idiosyncrasy, which makes him an exception to the general rule.'

"The action of the iodides in health, or in those who have some temporary or trifling complaint, is, in my experience, mostly a matter of dosage.

"When given in doses of 1 to 3 grains three times daily, running at the nose almost invariably is seen; but if the quantity be increased to 20 grains and upward three times a day, the coryza at once ceases. I am unable to offer any explanation of this marked difference in the action between large and small doses. Brunton‡ refers to this difference, and I believe that it is a very common experience.

"I have had no experience of the action of very small doses in chronic syphilis. I have no doubt that such a test would be instructive, and would possibly throw some light on the questions in dispute.

"There are two diseases where the iodides are usually given in considerable doses and for lengthened periods, and where there is, as far as I am able to determine, the same degree of immunity from iodism as there is

in syphilis. I refer to aortic aneurism and chronic lead-poisoning. Dr. George W. Balfour, of Edinburgh, who probably has had more experience with iodide of potassium in aortic aneurism than any living author, says,§ that he has only twice seen cases of complete intolerance of the iodide.

"Dr. George Ross, of Montreal, who has treated a large number of cases of aortic aneurism with iodide of potassium, says that it is a very exceptional occurrence to find any symptoms of iodism.

"It must be admitted that in a certain proportion of cases of aortic aneurism the patient is syphilitic.

"I have treated, during the past five years, upward of twenty cases of chronic lead-poisoning, and in not one instance is there any record of any iodism, and, with the exception of one case, there was no history of syphilis.

"I believe that my experience of the subject under consideration warrants me in coming to the following conclusions:

"I. That the exceptions to the rule, that iodism is very rare in syphilis of the nervous system, are too numerous to admit of the proposed 'therapeutic test' as being of value.

"II. That in certain other diseases (aortic aneurism and chronic lead-poisoning) treated with iodides, we have as pronounced an immunity from iodism as we have in syphilis.

"III. That in health iodism is the rule only when very small doses are taken, while large doses quickly arrest the iodism induced by the small doses.

"IV. That the toleration of large doses (10 to 20 grains) in health is the rule and not the exception. The advent and *not* the absence of iodism proves the idiosyncrasy of the individual.

"JAMES STEWART,  
"Professor of Therapeutics and Lecturer on  
Diseases of the Nervous System in McGill  
College, Montreal."

"I have read with great interest the two contributions to the subject of the diagnostic value of the tolerance of the iodides in syphilis made by Drs. J. William White and H. C. Wood, of Philadelphia. Being asked for my view of the questions upon which they fail to agree, it is needful to admit at the outset that one is justified in speaking with hesitation on any point in controversy between two col-

\* Quoted by Lewin in his work "Untoward Effects of Drugs," p. III.

† Wood, H. C., THERAPEUTIC GAZETTE, December, 1888.

‡ "Pharmacology and Therapeutics," 3d ed., p. 253.

§ "Diseases of the Heart," 2d ed., p. 459.

leagues of such distinguished position and large experience.

"A personal quality in the statements which follow is almost unavoidable. My written records cover only about fifteen years of experience, both in private practice and in civil and military hospitals, the cases of patients having nervous complications of the disease being not separated from the thousands exhibiting other symptoms of syphilis. Of immediate practical value in this connection is the fact that during the last five years, both in private and consultation practice, nervous syphilis in all grades from milder to grave and even fatal cases, has become disproportionately frequent.

"It is proper to admit here that the more highly specialized a man's experience, the less competent he becomes, not necessarily but presumably, for a decision of questions involving comparisons between the subjects of such specialized and non-specialized study. In this view, Dr. Wood, it seems to me, has some advantage over both Dr. White and myself. Dr. Wood appeals, as ground for acceptance of his views, to a hospital experience in fifteen years of more than two thousand patients, between twenty-five and fifty per cent. of whom were victims of non-syphilitic nervous disease. During the same period of time, while not able to speak for Dr. White, I believe that my personal experience in non-syphilitic nervous disease has been in comparison with these figures not worth citing.

"Under the comprehensive and acceptable term 'iodism' are now included and accurately tabulated an enormous list of symptoms of iodic intoxication exhibited in almost every system and viscus of the body, including what may be termed a mimicry of almost every cutaneous disease in our nomenclature. No ampler and more exact exposition of the subject has been made than in the monograph entitled '*L'Iodisme*', written by Dr. Elizabeth Bradley, and published in Paris in 1887. In this excellent work are included all the cases referred to by Dr. Duffy, cited by Dr. White. Two of my personal memoirs on the bullous rash induced by the iodides are here summarized. A few contributions to the subject which have appeared at a later date are, of course, wanting,—e.g., Hallopeau's '*Report of Singular Cicatrisiform Lesions following an Iodide Exanthem*'; Taylor's paper (read before the First Congress of Physicians and Surgeons in Washington in 1888) on so-called '*Acne iodo-potassique Anthracoïde*'; and my

paper on '*Dermatitis Tuberosa due to Ingestion of the Iodine Compounds*', read before the same body at the same date with Dr. Taylor's.

"Recognizing, then, the very wide range of phenomena included under the term 'iodism,' Dr. Wood's position may be tersely stated as follows:

"a. The majority of persons in health cannot tolerate large doses of the iodides.

"b. A large number of persons in health can secure such toleration by careful graduation and increase of the dose.

"c. A notable exception may be found in a small minority of persons in health who enjoy complete toleration as the result of idiosyncrasy.

"The reverse of these propositions is also held to be, in the main, true; thus:

"a. The majority of syphilitic persons tolerate large doses of the iodides.

"b. Careful graduation and increase of the dose in syphilitic patients does not interfere with toleration.

"c. A notable exception may be found in a small minority of syphilitic persons who cannot tolerate the iodides as the result of idiosyncrasy.

"From these propositions it is inferred that when in any person toleration of the iodides in large doses is exhibited, the diagnosis of syphilis is warranted if symptoms are also present of obscure organic disease. In another paragraph Dr. Wood indicates that failure of production of iodism by sixty grains of the iodide of potassium ingested daily practically establishes a diagnosis of syphilis.

"As to terms here used, it is understood and agreed that for purposes of the present question the 'syphilis' of Dr. Wood's paper is nervous syphilis, belonging to the advanced, late, or gummatous stage of the disease, which, it is well understood, may occur in special cases speedily after infection.

"Dr. White urges effectively, *per contra*, that the indications for the free use of iodine do not exist until this advanced or later stage of the disease has been reached, when the blood and tissues are not demonstrably pervaded by an active and generalized virus; when this virus has become non-symmetrical, non-contagious, and in many cases non-transmissible; when, in point of fact, there is no virus which a poison can neutralize. In this he is in full agreement with most syphilographers, and might even have added, that a coarse test of any physician's expertise in the management of the disease is here

furnished, most general practitioners hastily employing the iodide at periods when the expert finds no indication for its use. But the impressive fact is not to be forgotten, that while not demonstrably in its later or even last stage a generalized disease, still, after syphilitic infection, some general and persisting effect has surely resulted upon the system at large, since a new infection is, for the immense majority of all patients, impossible. No one can verify the exactness of Colles's law in a series of years and cases without reaching the clear conviction that the mother of the syphilitic child, even though herself exhibiting no symptoms, symmetrical, contagious, or transmissible, even though under the influence of no demonstrable virus, yet exhibits completest and fullest immunity as against the infectious mouth of her syphilitic offspring.

"It must also be freely admitted in Dr. Wood's favor, that toleration of the iodides by the syphilitic patient by no means indicates relief of syphilitic symptoms, that many cases of severe nervous syphilis are benefited immediately by mercury when the largest doses of the iodides are apparently without value, that the sequelæ of syphilitic lesions may be as serious in results as those immediately due to the lesions themselves, and that sclerosis in syphilitic subjects is certainly not amenable to specific treatment. This much admitted, I find myself totally unable to agree with this eminent author that there is any antagonism between the action of the poisons of syphilis and the iodine compounds to an extent justifying diagnostic conclusions. For,—

"I. We may entertain the suspicion that if we only knew enough there need be no intolerance whatever of the iodides by any person. The mischief is, we do not know how to establish toleration for some patients, while we do know for some others how to compass this end. Any conclusions based on different methods of administering the drug in different periods of the life of one person must be practically worthless. Given a uniform method and uniform conditions, and the number of idiosyncratic patients becomes rapidly smaller. Of this I am thoroughly convinced by experience. A few years ago I began to use only one method of administering the iodides, and by this term it may be conceded that all parties to the discussion intend to designate chiefly the iodide of potassium. That method was to employ a saturated solution, one grain to the minim

of distilled water, given in milk, when that vehicle was not found to disagree as an article of diet with the patient to be treated. The dose was made, at the outset, not more than 5 to 10 drops; the increase was ordered every three or four hours; and in face of the chemical dictum lately set forth, that the drug should always be given fasting, it was ordered after a small quantity of food was ingested. In this way the larger doses, as high as eight hundred grains daily, have been reached. I note, in passing, that it is my conviction that the very largest doses reached have not seemed as valuable as those which may be described as 'large,' the majority of all brilliant results being attained, I think, by a dose within rather than beyond two hundred grains daily.

"Observance of a uniform method in scores of cases soon led to the conclusion that 'idiosyncratic' patients were far fewer than was at first supposed. Careful graduation of the dose, and elimination of the cases in which the patient, eager for aid, surreptitiously swallowed more than his dose, threw new light upon this question. Again, the marked idiosyncratic exceptions that were observed soon occurred with symptoms of intoxication not cutaneous in type. Violent abdominal pains, tumefaction of the belly, grave prostration, and indefinable nervous impressions, which patients found difficulty in describing, but which they referred to with evident horror,—these were of the class that proved exceptions to the rule. The symptoms of iodism strictly cutaneous in type and of the odd appearance which I have described in my papers, were of the sort generally to which Dr. White refers,—that is, suddenly occurring at the outset of administration of the drug, in non-syphilitic (often very young) patients treated somewhat awkwardly by general practitioners for eczematous and other diseases of the skin. Let me note, in passing, on this part of the subject, that of these cutaneous rashes, one, I am satisfied, is etiologically separated from all the others. Whether the others be reflex, vaso-motor, or tropho-neurotic phenomena, or whether they be in part due to abortive efforts at elimination of iodine by the emunctories, it is certain that severe forms of purpura, even at times alarming in grade, may ensue long after full toleration has been established, being displayed most conspicuously in the lower extremities and over the belly. This, there can be but little question, is due to weakness of the vascular capillaries

(probably induced by both syphilis and iodine intoxication long continued), a condition in the adult not greatly different from some of the reported forms of haemophilia due to inherited syphilis.

"II. The fact that most patients exhibiting the symptoms of nervous syphilis are in the early periods of adult life, when the tissues are far more tolerant of toxicants than in youth, late middle life, and old age, is not only in part explanatory of the fact urged by Dr. Wood as evidence of syphilis, but is to be considered in connection with

"III. The further fact that most victims of nervous syphilis are of the male sex. The reasons for this are so evident that they need not be enumerated. If, now, we compare the men in the vigor of this period of life, mostly in the third decade, stricken with nervous syphilis at the date of the fullest enjoyment of sound health for the average of their race, possessing good average powers of resistance to poisons, and having relatively coarse skins, with the twenty-five to fifty per cent. of Dr. Wood's hospital patients having non-syphilitic nervous disease, what do we find? We may assume that Dr. Wood's patients were of the class that other physicians find in other cities than Philadelphia, similarly disordered. He probably had his full share of cases of infants and children affected with infantile spinal paralysis, chorea, tubercular meningitis, hydrocephalus, convulsions, and other nervous disorders of that period of life. Certainly, as regards cutaneous symptoms of iodism, this furnishes, in my experience, the most favorable class for such exhibition. He probably includes in his statistics the cases of hystero-epilepsy and hysteria in women, more particularly in young women, and those of catalepsy with other affections of the nervous system peculiar to that age and sex. Surely we may consider these girls and young women with delicate skins as second in the list most liable to iodic cutaneous manifestations, little apt to enjoy tolerance of the drug. Lastly, we may name the senile patients with *ramollissement*, paralysis agitans, and similar disorders, including those in the fourth decade of life or later, exhibiting symptoms of *délire de grandeurs*. No one of the classes here suggested includes patients whose tissues have such power of resistance to poisons as those of our average male patients with signs of nervous syphilis.

"Lastly, IV., and this point has been touched upon above, the suddenness of attack of nervous syphilis in our average male

patient in the second decade of life brings him before his physician with a good reserve of vital energy to draw upon in an emergency. Possibly this furnishes in part the excellent statistical results of treatment in cases early recognized. If he lie in bed, apparently near his end, but actually destined to survive the natural expectation of longevity for his age, he has often a torso that might serve for a sculptor's model. He may drag a lower limb that would not deform a statue of Apollo, or, when taxing the English language for terms in which to eloquently describe his agonies of the night, exhibit a face that to all but the eye of the expert might pass for that of one in sound health. I have often been struck with the fact, that the average patient exhibiting marked syphilitic cachexia is not of this class. The cachectic is often the hospital patient presenting the most repulsive of the pictures in the gallery of deformities producible by lues. He may have what the farriers call a 'splint' on each leg from osteo-periosteal disease; his pinched and sallow features tell a pitiful story of malnutrition; the nose may be simultaneously flattening from caries of its bones; he may also exhibit half a dozen deep and formidable ulcerations from degenerating gummatæ,—and yet not suffer from any one of the many signs of nervous syphilis that may be fully shown in the next well-nourished patient under observation without an external stigma of disease.

"I conclude with the remark, that if Dr. Wood should come to me with the statement that he had under observation a vigorous male patient in the second decade of life, with an obscure disease of the nervous system, who was tolerating large doses of the iodide of potassium so well that a diagnosis of syphilis was practically established on that basis alone, and that the reason for the tolerance was an antagonism between the virus of syphilis and the poison of the iodide, I should respond: 'Granting the exactness of your hypothetical diagnosis which, in any event, I regard as well placed, one is justified in believing that your patient tolerates well the remedy you have employed, because he is what he is, syphilis wholly excepted.'

" JAMES NEVINS HYDE,  
" Professor of Dermatology and Venereal Diseases in Rush Medical College.

" CHICAGO, January 5, 1889."

" NEW YORK, 5 WEST FIFTIETH STREET,  
" January 10, 1889.

"MY DEAR DOCTOR WHITE,—In answer to your request for my opinion in regard to the diagnostic value of a toleration of large doses of the iodide of potassium in determining the presence of syphilis, and also the reasons for that opinion, I reply to the first by an expression of my belief that such toleration is wholly valueless as a proof of the present or antecedent existence of syphilis in any case. As to the reasons for this opinion, I wish to say that, during an experience of over thirty years in the study and treatment of syphilis, I have met repeated cases where the iodide of potassium has been administered up to a drachm three times a day with easy tolerance in individuals suspected of having syphilis, but in whom there was no positive evidence of the existence of the disease in its early or late forms, and where the subsequent history confirmed this position. I have also myself, in testing cases where the diagnosis was doubtful as between cancer and syphilis, repeatedly found the highest tolerance in cases which subsequently proved to be cancerous. On the other hand, I have met many cases of unquestionable syphilitic origin where the most marked intolerance of the iodide of potassium was present; where from 5 to 10 grains, thrice daily and largely diluted, would promptly produce some form of iodism. In one case in particular, which I shall not readily forget, 10 grains of the drug, thrice daily for a week, produced œdema of the pharynx and glottis, which nearly proved fatal. I have at the present time under observation two cases, who have an undoubted syphilitic history, where any attempt to raise the dose above 10 grains produces coryza and indigestion within a few days to an extent making its continuance unbearable; and again another, where 5 grains produce an unpleasant aching in the parotid and submaxillary glands within an hour. I have also seen repeated cases of grave cerebral trouble where a claimed intolerance of the iodide of potassium has been the basis of a diagnosis excluding syphilis, and yet where, by varying the methods of administration of mercury and the iodide of potassium previously pursued, these remedies have been tolerated to the extent of producing manifest improvement, and in some cases even cure. Prominent among my records is a case coming to me from a distinguished specialist in mental diseases, where, because of the apparent intolerance of both mercury and the iodide of potassium, the case

was pronounced one of the melancholic forms of general paralysis of the insane, non-syphilitic, and hence hopeless. Under a more careful and persistent effort, resulting from positive knowledge of a previous syphilitic infection, a toleration of both mercury and the iodide of potassium up to the full physiological effects of each resulted in rapid and apparently complete recovery,—the patient being now (January 10, 1889) in perfect bodily and mental condition, and having been so for nearly two years.

"A few words in regard to the reasons which seem to me to support the results of my clinical observations. The late lesions of syphilis are especially in question. Professor Wood says, on page 12 of your discussion, that '*the tolerance of the iodides belongs to the advanced rather than to the early stages of the disorder.*' The late lesions of syphilis (*sequelæ*) can, I think, be reasonably shown to be always *local* in their nature and development, and always to begin by a deposit of the so-called 'gummy' material. This scientific investigation has shown to consist chiefly if not wholly of germinal material, and in no way different from that of normal origin.\* In further proof of this position is the fact that, under favorable circumstances, it is capable of organizing into fibrous or cicatrical tissue. Subjects of gumma are ordinarily quite well, except from the mechanical effects of its presence. The children they beget are free from any syphilitic taint.† The removal of the gumma, wherever situated, may be effected by the efficient use of the iodide of potassium alone, resulting in a prompt disappearance of symptoms, and, if the removal of the deposit is complete, there is likely to be no return. But if more or less sclerosis has occurred, the use of the iodide is found to be inefficient. This agent seems not to be of sufficient power to produce fatty degeneration, to remove the deposits after a certain degree of organization has taken place. In such cases mercury is found of greater efficiency,—not because it is an antidote to syphilis, but because it is the most powerful of all known agents in producing fatty metamorphosis. No increased tolerance of mercury is claimed in persons the subjects of syphilis. The physiological effect of

\* See "Cornil on Syphilis," translated by Professors Simes and White, page 206. Lea & Co., Philadelphia, 1882.

† See Fournier, "On Syphilis and Marriage," page 231. Paris, 1880. Also Otis, "On Syphilis and the Genito-Urinary Diseases," page 171. Putnam, New York.

mercury consists simply in a more or less pronounced fatty degeneration of healthy tissues, first observed in the mouth and adjacent gland-structures. This occurs quite as promptly in the syphilitic as in the non-syphilitic. There would appear, then, to be no especial reason why the iodide of potassium, which apparently acts upon the late lesions of syphilis practically in the same way, should be credited with a salutary antagonism to a poison which is fairly well proven to have no existence in the so-called tertiary or late stages of syphilis. I feel confident that further careful observation of the nature and treatment of syphilitic disease in its various stages and sequelae will show that the antidotal view of remedies in syphilis is untenable, and that the medicines and measures which prove most useful in the treatment of this disease will be found in no sense peculiar in their effects upon persons who have, have had, or who have not had syphilis.

"Very truly yours,

"FESSENDEN N. OTIS,

*"Professor of Genito-Urinary Diseases in the College of Physicians and Surgeons, New York."*

"DEAR DOCTOR WHITE,—A careful reading of the pamphlet sent me leads to the inference that the 'question at issue' referred to in your note of December 28, 1888, and concerning which you request my opinion, is fully embodied in the following sentence quoted by you from Dr. H. C. Wood: 'In all cases of doubtful diagnosis the so-called therapeutic test should be employed, and if sixty grains of the iodide of potassium per day fail to produce iodism, for all practical purposes the person may be considered to be a syphilitic.' Now, if I am asked whether I consider this broad rule of action sufficiently reliable to form the basis of a diagnosis, I reply that I do not. I believe that its application in practice in doubtful cases would lead to error in two directions:

"1. By leading to a diagnosis of syphilis when that disease was not present; and,

"2. By failure to diagnosticate the disease when it was present.

"And, furthermore, I believe that either of these errors would occur so frequently as to seriously vitiate the result. The fact that they lead to error in opposite directions doubles the ultimate effect and all the more confirms me in the opinion that the rule itself is *fallicissima res*.

"It seems hardly necessary to say that my

belief is based upon my observations of the frequency of the occurrence of iodic intoxication ('iodism') in cases of late—that is, the so-called tertiary—syphilis. Only exceptionally do I give the iodides in the earlier manifestations, and this for the reason that they are not then needed; but I do give them, and find that they produce 'iodism' as frequently as in the later stages, but not more so. In what I have to say here in relation to the value of the non-appearance of 'iodism' as a diagnostic of the existence of syphilis, let it be understood that I confine myself to the employment of that drug in the later stage. Also, let me say that, for present purposes, the term 'idiosyncrasy' is held to mean an individual peculiarity which causes a certain proportion of our patients to exhibit symptoms of the toxic effect of the drug when given in moderate or small doses, while 'iodism' should include 'the various forms of iodic intoxication, the most common of which are gastro-intestinal irritation, coryza, lachrymation, mental depression, tinnitus aurium, and a pustular eruption (acne) upon the cutaneous surface.' With this understanding, I am quite within bounds when I say that fully fifty per cent. of the cases of late syphilis treated by me exhibit iodism long before sixty grains per day is reached. In fact, it is only in a minority of the cases that *some* of the toxic effects fail to show themselves before a dose of thirty grains per day is reached. If we include all the untoward effects of the iodides which we see in the eyes, nose, pharynx, fauces, mouth, stomach, skin, and nervous system under the term iodism, I cannot make out that the size of the daily dose bears any relation whatever to their appearance. So far as I can see in practice, a given patient who bears 5-grain doses thrice daily, without any toxic effect, will bear equally well 20-grain doses repeated at the same intervals. My own observation, then, accords with the assertion of Jonathan Hutchinson, that the size of the dose bears no relation to the frequency of the toxic effects. The most dangerous case of iodism which I ever had in my practice followed quickly upon a 3-grain dose. When an important viscus (brain, liver) is threatened, or when any organ is having serious damage wrought in it by syphilis, I do not suppose that any one would be deterred from pushing the remedy by the occurrence of a minor evidence (acne, coryza) of iodic intoxication. And, perhaps, after all, here lies the reason for the great

discrepancy of evidence in this matter. Patients often overlook the minor evidences until attention is called to them by the physician; and it seems to me to go without saying that cases of cerebral syphilis would be vastly more apt to do this than any others.

"That there is wide difference of opinion in regard to the relative tolerance of the iodides by the syphilitic and the non-syphilitic, as well as in the views of different observers and investigators as to the means to be resorted to to determine the question, there can be no doubt. Upon one point, however, there is practical unanimity of opinion, as indeed there could not help being: this is the fact that 'iodism' does appear on the administration of moderate, even small, doses of the drug to patients who we know have syphilis in the later stages. Here there is common ground upon which all may meet and fight the battle out, even if figures are to be the weapons. Meeting here, it will make no practical difference whether syphilis in any stage increases the tolerance of the iodides. The question will then be, whether 'iodism' occurs frequently enough in syphilites to render the rule quoted above ineffective for diagnosis. I believe it does. If this view is the correct one, then any discussion of the question of tolerance, highly interesting as it is, is of no practical use in the determination of the diagnostic point. If the question of this 'idiosyncrasy' can be eliminated by reason of its infrequency, then the matter of relative tolerance will be of high value.

"Figures as to this frequency of iodism in syphilites I confess my inability to give, for the reason that neither at my clinic nor in my private practice have cases been recorded with this question in view; and I do not believe that the mere relation of such few cases as I now have in mind would accomplish the object sought.

"Very sincerely yours,

"JOHN P. BRYSON,

*"Fellow of the American Association of Genito-Urinary Surgeons.*

"ST. LOUIS, January 28, 1889."

"PENNSYLVANIA HOSPITAL FOR THE INSANE,

"PHILADELPHIA, January 25, 1889.

"DEAR DR. WHITE,—I have read the reprint of a discussion between yourself and Dr. H. C. Wood, taken from the *THERAPEUTIC GAZETTE*. The proposition which Professor Wood has announced is likely to attract attention, both on account of its novelty and

because it is a very positive statement about a subject that is considered obscure and unsettled. If Dr. Wood's views turn out to be correct eventually, his present position certainly is that in which some of our legal friends find themselves,—with a good theory of law on their side, but not the facts to sustain it. The vigorous and temperate tone of the discussion is most commendable. A general response to the questions growing out of the discussion and the questions announced in the *THERAPEUTIC GAZETTE* cannot fail to throw much light upon this subject.

"Referring to exact data in my own experience, it may be stated that, at the present time, of three hundred and ninety patients in this hospital, one and a half per centum have such a history of syphilis that their insanity may be fairly attributed to that cause. From observation in hospitals for the insane outside of cities, the proportion does not seem to be as great, if we exclude paretics. In the production of paresis syphilis is as yet an unknown factor. The departments of a city almshouse hospital contain a population deteriorated by a low heredity and broken down by various vicious indulgences, that 'tolerate' medication to an extraordinary extent, as a rule. It is an element to be considered in deductions made from observations among this class, and might otherwise form a source of error.

"I recall five cases in which the insanity resulted from syphilis where the iodide of potassium was administered to the extent of forty-five and eighty grains daily. The medicine was discontinued because it produced gastro-intestinal irritation. In 1857 I reported a case of insanity from syphilis that recovered under the use of iodide of potassium in 5-grain doses three times daily. One case recovered in this hospital under the use of one hundred and eighty grains daily, and another made a good recovery taking eighty grains daily.

"So far as these cases go to establish any result, the majority show that extraordinary doses were not borne, and the medicine was discontinued, and in one case that a small dose accomplished as much as a large dose did in another case. But it may be said the diagnosis of these cases was not in doubt. It is conceded they were not, yet they show that a small dose and moderate doses sometimes accomplish the desired result as well as extraordinary doses; also, that the known existence of syphilitic disease did not prevent iodism, even in moderate doses.

"We are told, however, that in all cases of doubtful diagnosis, if the so-called therapeutic test is employed without producing iodism, the person may be considered a syphilitic. Does such a test commend itself to our best judgment as conclusive? Having administered large doses of a drug to a doubtful case, and not poisoned our patient or produced any other result, perhaps, are we to conclude he is a syphilitic? What has occurred to solve our doubts? Are our results not wholly negative, and is not an opposite conclusion equally legitimate? Is it true that in these tertiary cases we are contending against an active virus that is said to neutralize large doses of the iodide, or are we not rather seeking in our treatment to remove the results of the virus in its active stage, as we aim to remove the results of a meningitis, and exudations in other diseases? Cases of chronic rheumatism, obscure mental and nervous diseases, and meningitis occur which bear large doses of the iodide. Must we for this reason conclude they are syphilitic? If in a doubtful case the iodide cures our patient, our doubts may be said to be removed. But can it yet be said to be settled that the existence of syphilis was established? If we administer the iodide in a doubtful case and have no result and have not poisoned our patient, we have only established the fact that no idiosyncrasy exists,—perhaps nothing more. I cannot concede that a new principle can be said to have been evolved from what has yet appeared. If it has been and will stand the test of experience, it must have a wider application in the practice of medicine than that which has been made of it to the class of cases in question.

"Very truly yours,

"JOHN B. CHAPIN,

*"Physician in charge of the Pennsylvania Hospital for the Insane."*

"PENNA. HOSPITAL FOR THE INSANE,  
"DEPARTMENT FOR MALES, January 26, 1889.

"MY DEAR DR. WHITE,—I am under many obligations for the opportunity of reading the 'Discussion' between Dr. Wood and yourself.

"In answer to your request for my opinion upon the question at issue, I do not know that I can say anything which will add to the interest or value of the discussion so ably opened. At the same time, I must say that I have pretty firm and definite opinions based upon considerable experience with syphilis in its ordinary manifestations, as well as with so-called nervous syphilis.

"The late effects of syphilis, especially in the way of nerve-lesions, have interested me ever since my entrance upon the practice of physic. Indeed, my inaugural thesis was upon 'Syphilitic Affections of the Nervous System.'

"It seems to me that to base a diagnosis of syphilis upon the tolerance of large doses of the iodide of potassium, in cases in which the diagnosis was otherwise obscure and doubtful, would be unwise and at variance with the judgment and experience of the profession. I was long ago taught, in cases where the least doubt existed, and where its administration was not contraindicated by other conditions, to give the iodide, and to push it to the limit of toleration where such heroic treatment seemed desirable; but I have never ventured to diagnose syphilis, even in cases brought to a successful issue, because of the success; much less would I feel justified in so doing because of mere tolerance of any particular drug.

"If Dr. Wood means to say that few normal individuals (free from syphilis?) can tolerate sixty grains of the iodide a day, if at once placed upon that amount, I see no reason for differing materially with him; but still I am sure that there are numerous individuals who are, as far as syphilis is concerned, normal, who can rapidly be brought to take sixty, eighty, and ninety grains of the iodide a day. On numerous occasions I have prescribed at once 20-grain doses, to be repeated three times daily, and the instances in which any intolerance was shown were exceedingly rare. I cannot be induced to believe that all these cases who had a tolerance for the drug had syphilis; indeed, I know that many of them did not. It has been my habit for years, in prescribing the iodide, to commence at 10 grains, and, when desirable, to increase by adding one grain a day to each dose, the doses being given three times daily at least. The records of numerous cases which have occurred since my connection with this hospital do not show a single instance of iodism or anything pointing in that direction, except in one markedly syphilitic case (initial lesion in 1868), who had a profuse crop of acne after taking 10 to 13 grains three times daily for a few weeks.

"This case leads me to refer to another, in which there was a peculiar idiosyncrasy. I saw the patient, a medical man, in the spring of 1873, suffering from a neurosis of evident syphilitic origin. This patient could not take 20 grains of the iodide in solution three times

daily without having marked coryza, disturbance of digestion, etc., but he was able to take 96 grains in pill form three times daily for weeks with no ill effects.

"It may be answered that of these large doses a considerable proportion passed off by the bowel. The result proved the contrary, as rapid improvement occurred under the treatment by the pills, which had not taken place under its persevering use in solution. It would certainly have been wrong to have excluded syphilis because of the non-tolerance of the large (20 gr.) doses in solution.

"About the same time I saw a gentleman whose case had been progressively growing more serious, notwithstanding active and apparently judicious treatment. He had insomnia, great pallor, emaciation, and general malaise. There was no suspicion of syphilis, had never been any exposure, and the gentleman had no object in concealment; moreover, he knew the importance and bearing of the questions regarding syphilis which were put to him. His only heredity was a gouty diathesis. Under the use of the iodide of potassium, commencing at 20 grains, and rapidly increasing the dose to 60, and then to 90 grains, three times daily, this patient put on flesh, gained in color and strength, and eventually made a good recovery. The exact pathological condition was never diagnosed, but certainly syphilis must be excluded.

"I have administered, or seen administered, large doses of the iodides in cases of goitre, in certain rheumatic affections, in plastic pleurisy, in the treatment of aneurism after Balfour's suggestion, and in varied affections of the brain, chronic meningitis, tumor, acute hydrocephalus, etc., and while I cannot now refer to figures, I am confident that the tolerance of the drug was as great in non-syphilitics as in syphilitics. I speak with some confidence on this point, for the reason that long ago I established the rule of impressing upon persons whom I had treated for syphilis the importance of always in any subsequent illness informing the attending physician of the constitutional taint, and in cases which came under my care or observation with other diseases, I have been equally careful to inquire as to specific infection.

"In cases of insanity the history is often obscure, for the reason that the only person who could affirm or deny the suspicion of syphilis is not in a state to give reliable testimony, but something over ten years of pretty active service in this field has not given me

any data to confirm Professor Wood's theory. I have been in the habit of using during that time doses of the iodide, ranging from thirty to three hundred grains daily, in syphilitic and non-syphilitic cases, but I feel as confident as I do of any conclusion drawn from experience, that the tolerance in syphilitic cases was not sufficiently marked, as compared with non-syphilitics, to offer any grounds upon which to base a theory or make a diagnosis.

"I do not know of any reason for supposing that the tissue-changes from syphilis are alone of such a character as to cause a tolerance of the iodides in the animal economy, if we admit even that such tolerance may be produced by disease. An examination of the facts would seem to indicate the contrary, as well as when we argue from theoretical grounds alone. No disease yields so readily to medicine as late syphilis does to the iodide of potassium, and yet Professor Wood asks us to believe that the very drug which has such a power over the disease is rendered by that disease innocuous to the body in which the disease resides.

"I do not see that anything is to be gained by Professor Wood's suggestion, as much as I am loath to differ with so able and experienced an observer.

"If syphilis cannot be diagnosed by other means, why is it necessary to call the case syphilitic because a drug successfully employed in the treatment of syphilis is tolerated, or even brings about a recovery? If mere toleration is all that is observed, nothing is gained, surely; and if recovery takes place, what advantage is there in knowing that 'for all practical purposes' the case was syphilitic?

"If the iodide of potassium had no remedial power except in syphilis, a diagnosis might be safely made after successful treatment; but mere tolerance of the drug would give no safe and proper ground for judgment. It seems to me that nothing is to be gained, and some risk at least of injustice to the patient is incurred by such reasoning.

"Very sincerely yours,

EDWARD N. BRUSH,  
"Assistant Physician Pennsylvania Hospital for  
the Insane."

"January 30, 1889.

"DEAR DR. WHITE,—The keynote to the discussion between yourself and Dr. Wood seems to me to hinge upon the latter's statement that 'In all cases of doubtful diagnosis (of cerebral syphilis) the so-called therapeutic

test should be employed, and if sixty grains of iodide of potassium per day fail to produce iodism, for all practical purposes the person may be considered to be a syphilitic.'

" Leaving out of the question, for the sake of brevity, the intimate changes induced in the system by the iodides and the nature of the syphilitic person, I will briefly give you the result of my observation and study of the action or rather behavior of these drugs.

" In the first place, I must protest against the current idea of confounding idiosyncrasy with intolerance. Very many persons have an idiosyncrasy against the iodides, but in very few is there an actual intolerance. This is particularly fortunate for them and for us.

" As to the action of the iodides in non-syphilitics my experience has convinced me that these salts are well borne by very many patients of both sexes and of all ages. In some, however, they produce such lesions and affections as dermal inflammations, coryza and lachrymation, edematous swelling of the parts supplied by the fifth nerve, cerebral hyperæmia, mental and physical depression, and gastro-intestinal irritation.

" Of these cases, it may be said,—

" 1. That they may be persistent even when all possible means of amelioration have failed.

" 2. That in many instances, if the drug is pushed, notwithstanding perhaps some discomfort to the patient, these unpleasant and sometimes alarming phenomena will cease and the drug will be not in any way harmful and actually beneficial.

" 3. In some of these cases we, as they say, 'weaken' too quickly and give up the drug, whereas, if with proper moral courage (the urgent necessity of course existing) we increase the dose and go ahead, toleration is established. In many cases in my experience *small initial doses* have produced mischief, while the succeeding larger ones have been very acceptable.

" 4. In many cases, abstinence from liquors, alcoholic and fermented, care as to the simplicity and easy digestibility of the food, requisite medication for the stomach, and a general improvement of the alimentary canal will be followed by a proper acceptance of the drug, perhaps with some preliminary skirmishing.

" 5. I have seen several cases in which the iodides were well borne, previous to the onset of pathological changes in the kidneys, and after the evolution of the latter they were more or less toxic in their action, sometimes so much so that their administration was of necessity suspended.

" 6. I call to mind three cases in which, while the patients were high livered and deep drinkers (one exclusively of champagne), the iodides were not borne without great discomfort, but when they discarded these irritants and stimulants, the iodides produced no discomfort (cerebral, dermal, nasal).

" 7. I have seen cases in which an intolerance of the iodide of potassium lasted twenty years, and at both ends of that period produced a characteristic bullous eruption.

" My experience has not convinced me that syphilis gives a man any immunity, partial or complete, to the toxic action of the iodides. Indeed in general the experience I have already detailed with virgin subjects applies to syphilitic individuals. The secret of very many cases rests in the fact that dire necessity compels the continuance of these drugs, and the so-called intolerance is forgotten.

" In syphilitics as in healthy subjects an intolerance of to-day may be replaced by a condition of assimilation a month, a year, or several years hence.

" I call to mind the case of a man who had gummatous infiltration into the soft palate, and seemed intolerant of the iodide of potassium. I pushed it, however, and his intolerance ceased before the infiltration was absorbed. Four years later (after a life of great indulgence) he had syphilitic pachymeningitis, took heroic doses of the iodide, showed no intolerance, and got well.

" I strongly suspect that many cases which have led Dr. Wood to formulate his therapeutic test are like the one just mentioned, and that a previous course of the iodides has conquered the intolerance which may have existed in them.

" In this connection I would call your attention to the case of 'Dermatitis of Iodic Origin,' reported and figured by me in the *New York Medical Journal*, November 3, 1888. The patient, three years syphilitic, suffered from nocturnal pain in the head, not localized but more severe in the forehead and eyes. For six days he took twenty grains of the iodide thrice daily, for six days longer he took twenty-five grains, then the dose was increased to forty grains, with the effect of producing in fifteen hours one of the most severe forms of iodic eruption known. The necessity, however, existed for still larger doses, and he got them without any intermission. The dermal lesions ceased and he lost his pain in the head. He had enlarged spleen but healthy kidneys.

" In conclusion, after a careful study of your

papers and of Dr. Wood's rejoinder, leaving out of consideration all hypotheses and judging from the facts of observation and study as far as I am able to do so, I must say that I think that your three postulates stated upon page 8 of your pamphlet are sound.

"Very truly yours,

"R. W. TAYLOR,

*"Professor of Venereal and Skin Diseases in the University of Vermont."*

"16 WEST THIRTY-SECOND STREET,  
"NEW YORK CITY.

"DEAR DOCTOR,—With regard to the question upon which you have done me the honor of asking an opinion, as to the diagnostic value of the tolerance of the iodides in syphilis, I believe that the idea, which is still quite prevalent, that if a given obscure lesion disappears under the use of the potassium iodide, or if the iodide is tolerated in large doses, that therefore it must be syphilis, is a fallacious and misleading one. Too much stress has, I think, been laid upon the touch-stone theory of the action of medicines, and in none more than in the results obtained from the use of mercury and iodide of potassium.

"Putting to one side for the moment those cases of syphilis in which organic lesions have occurred and where no good has ensued from the administration of large doses of the potassium iodide, although they have been well borne, there are other cases where the same tolerance of the drug is shown in which the disease is not syphilitic, as witness cases of cyclitis, gouty affection of the joints, and the like. Here the iodide often acts like a charm; and although the question may be raised whether the lesions are not really due to syphilis, notwithstanding that no history or evidence of the disease exists, still I think that does not invalidate the correctness of the diagnosis, and the maxim '*de non apparentibus*' may be fairly invoked in support. Again, if the effect of the iodide in syphilis is to be taken as a guide or index of the nature of the affection under consideration, how is it that in the earlier stages of syphilis the iodide is not so well borne and is more liable to produce disturbance than when given in the later phases of the disease? And yet such has been my experience, and no doubt the experience of others.

"Taking the reverse of the proposition: idiosyncrasy often acts in such a manner as to preclude the administration of the potas-

sium iodide, and still the disease remains syphilis; yet were the rule—that if the iodide is not tolerated therefore the disease cannot be syphilis—acted upon, the surgeon would be led into error, to the detriment of his own reputation and his patient's welfare.

"In Dr. Wood's paper I see that he also has found that patients showing the early stages of syphilis do not stand the iodide as well as those who are in the advanced stages of the disease, and in so far I agree with him, but there are one or two points upon which I should take issue with him. On the 12th page he writes: 'The production of iodism by small doses of the drug is, however, evidence (not proof) that the patient is not suffering from syphilitic disorder, and in any given case renders it probable that the symptoms are not the result of syphilitic infection.' My opinion is that such a condition would be neither evidence nor proof that the disease was not syphilis, for I have found that small doses of the iodide, and that in syphilitic persons, will more readily produce the toxic symptoms of the drug than when it is administered in large doses,—and by small doses I mean 20 grains or under, and by large ones above that amount. To my mind, therefore, the small dose is no test.

"On page 15 he writes of the slowness in action of the iodides. My own experience points in the opposite direction, for, if I desire to get a quick result in checking the extension of an ulceration or the increase of a gummosous growth, my first weapon is large and liberal doses of the potassium iodide; but one point, which should be borne in mind as regards the good to be obtained from the use of the iodide, is that its action is limited, and it is not, to my mind, a curative agent in the treatment of syphilis. It is an adjuvant to mercury and an admirable assistant in many cases, but it is not the right bower, hence what Dr. Wood observed in the autopsy of his epileptic patient—recorded on pages 15 and 16—is what should be expected. He is quite right when he goes on to say that 'more and more has it come to be with me a favorite rule of action in cerebral syphilis, without evidences of cachexia or a distinct history of mercurialization, to begin the treatment with mercury,' but I think he is not so much in the right when he goes on to say 'in such doses as to cause slight salivation, and to maintain this impression for some days or weeks *pro re nata*.'

"In no cases of syphilis do I believe it necessary to induce ptyalism during the course

of treatment ; indeed, I am inclined to regard it as a disadvantage rather than a benefit. Nor do I, as does Dr. Wood, consider it necessary to administer the iodide after a mercurial course in order to produce elimination of the mineral, for I believe the mercury is promptly eliminated by itself if the drug be properly administered.

"And now, dear doctor, I think I have stated my opinion on this interesting subject, as you have asked me to do ; and with many apologies for my delay in replying, believe me,

"Very sincerely yours,

"F. R. STURGIS,

"Professor of Venereal Diseases in the Medical Department of the University of the City of New York."

" 2 WOODSIDE TERRACE, GLASGOW.

"MY DEAR SIR,—In reply to your letter of 6th January, I have to say that, in my experience, the occurrence of the phenomena of iodism depends upon idiosyncrasy. I have often given the iodide of potassium in very large doses, even to the extent of two ounces daily, to non-syphilitic subjects (*e.g.*, to patients suffering from undoubted non-syphilitic psoriasis, and from aneurism without syphilitic antecedents), without any unpleasant symptoms, and I believe that iodism results much more frequently from small than from large doses.

"I have frequently observed iodism set in, and generally soon after the medicine was commenced, in syphilitic subjects, both in the secondary and tertiary stages, and have found it occur just as frequently in syphilitic as in non-syphilitic persons. So that I entirely agree with you in placing no confidence in the diagnostic value of the tolerance of the iodides in syphilis.

"Yours, sincerely,

"T. McCALL ANDERSON,

"Professor of Clinical Medicine in the University of Glasgow.

"To J. WILLIAM WHITE, M.D.

"January 18, 1889."

" NEW YORK, January 2, 1889.

"DEAR DOCTOR,—I consider Professor Wood's statement that 'if sixty grains of iodide of potassium per day fail to produce iodism, for all practical purposes the person may be considered to be a syphilitic,' to be a dangerous generalization, likely to lead

to looseness in diagnostic methods, to say nothing of the moral aspect of the question.

"I have neither time nor inclination to discuss the subject here, but my belief is that the whole matter of the tolerance of iodides is personal with the individual, that this personality is not modified by syphilis, but it may and does change in some individuals, and that too without the intervention of syphilis.

"This is my general view, which I could sustain at length, but that I am overborne at this moment with a multiplicity of duties and responsibilities.

"Yours truly,

"EDWARD L. KEYES,

"Professor of Genito-Urinary Surgery and Syphiliology in Bellevue Hospital Medical College."

" BUFFALO, January 1, 1889.

"MY DEAR DOCTOR,—I don't think my views on the subject of your recent paper are worth perusal, but I am inclined quite strongly to the opinion that iodism is a matter of idiosyncrasy vastly more than of dose, particularly those severer forms which prevent its administration. Jullien's theory appears to me untenable.

"I see very few cases of purely nervous syphilis, but I should hardly act upon Professor Wood's theorem for a working basis. The cases to which he refers are the uncertain cases, where diagnosis is either difficult or impossible. The disappearance of the symptoms under the iodides (one drachm per diem) might be presumptive evidence in favor of their specific character, but I should be loath to accept the statement that one drachm per day would cause iodism unless the case were syphilitic,—providing that by his expression 'iodism' he meant something more pronounced than a few pustules on the face, etc. And even in case he includes under 'iodism' the slightest manifestation I should consider it too sweeping a statement.

"Perhaps we all view the matter from the specialist's stand-point, but I am inclined to coincide with the views expressed by yourself. I have in mind a few cases which give me a present reason for my convictions, and yet not one of those I now call to mind was under personal observation for a sufficient length of time to justify any other use of it than to put it in a group with others and try to thus make it of some aid.

"As one who deals with the surgical aspect

of these cases oftener than with their uncomplicated drug-treatment, I may be excused from allowing your complimentary request for my opinion to put me in a position where I might find myself without adequate means of defence.

"Sincerely yours,

"ROSWELL PARK,

"*Professor of Surgery in the Medical Department of the University of Buffalo.*"

"DEAR DOCTOR WHITE,—The point at issue between you and Dr. H. C. Wood I take to be, Whether tolerance of the iodides in a given case is, *quoad syphilis*, of diagnostic value? I confess to have shared the widely-spread belief in the affirmative proposition, but in looking over my notes I find no data from which I can glean a positive answer one way or the other. I find two groups of cases in which I have given the iodides in large doses, —cerebral syphilis and aneurism. Certainly patients with the former affection bear, as a rule, very large doses, which may be kept up for months, but I call to mind two cases at least in which this tolerance existed, and in which the lesions proved, post mortem, not to have been specific. On the other hand, I

have seen instances of undoubted syphilis in which intolerance of the iodides was a striking and persistent feature.

"Some years ago I was in the habit of giving large doses of iodide of potassium in cases of aneurism, and I have frequently referred to the apparent tolerance of the drug presented by these patients, yet the case which bore for the longest period—three months—the largest doses had not had syphilis.

"I am inclined to regard intolerance as a matter of idiosyncrasy, and should say that, while a large proportion of all patients bear the iodides in full doses for long periods, a small number cannot take even minimum doses without unpleasant symptoms. The 'general impression' which I have had as to the tolerance of the iodides in syphilis has no doubt resulted from the fact that I have given large doses for long intervals in this disease, and in aneurism, so often associated with syphilis. I willingly acknowledge this impression to be worthless in the absence of control-observations of equal number in other diseases.

"Yours sincerely,

"WM. OSLER,

"*Professor of Clinical Medicine, University of Pennsylvania.*"







